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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/675,592	09/30/2003	Sergey Dzekunov	MAXC:014US	9928

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EXAMINER	
FERNANDEZ, SUSAN EMILY	

ART UNIT	PAPER NUMBER
1651	

MAIL DATE	DELIVERY MODE
10/03/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/675,592	DZEKUNOV, SERGEY	
	Examiner	Art Unit	
	SUSAN E. FERNANDEZ	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-8,12-16,34 and 35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *34 and 35* is/are allowed.

6)☒ Claim(s) *1,3-8 and 12-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/13/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed April 18, 2008, has been received and entered.

Claims 1, 3-8, 12-16, 34, and 35 are pending and examined on the merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-8, and 12-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Calvin (US 5,098,843) in view of Mehta (US 6,122,599) and in light of Torr et al. (US 6,891,712).

One of the embodiments taught in the Calvin patent is a continuous flow electroporation method wherein cell suspensions are pumped through an electroporation chamber shaped so that "...the high intensity electrical field to which the cells are exposed varies in intensity..." (column 7, lines 22-34). Figures 5 and 6 demonstrate this embodiment of the Calvin patent. Given that the electric field is created by a pair of electrodes shaped to line a venturi passage (column 8, lines 4-12 and see 100a and 100b on Figure 6), the electric field generated is inherently spatially inhomogeneous. See Torr et al., column 5, lines 31-37, which points out that inhomogenieties of electric field lines can be achieved with a system of electrodes with curvature to the surfaces.

In the practice of continuous flow electroporation in a continuous flow electroporation chamber, "...a potential of 600 volts DC **is maintained** by power source...on the electrodes within the chamber" (column 7, lines 58-62, emphasis added). Since the voltage is maintained at 600 volts DC, the electric field is substantially constant in magnitude and the electrodes are continuously energized while the cell suspensions traverse the electric field. Moreover, Calvin even points out that "where continuous flow methodology is practiced, the desired effects of a transient high intensity electric pulse are simulated by varying and controlling the flow rates of the cell suspension as such suspension travels through an electroporation chamber having a venturi shaped passageway including appropriately shaped electrodes impressed with a high level of DC voltage" (column 2, lines 61-68, and see also column 8, lines 35-41). Clearly electric pulses are not applied to the suspension while it traverses the electroporation chamber as the act of sending the suspension through the chamber simulates an electric pulse. Thus, limitations recited in instant claims 1, 2 (electrodes must be coupled to an electric current source in order to provide an electric current voltage), 6 (duty cycle must be about 100% in order to maintain a potential of 600 volts DC), 7, 8, and 16 are disclosed in Calvin.

Calvin differs from the claimed invention in that it does not teach the application of AC voltage wherein polarity of the electric field is periodically reversed and the electric field is established by electrodes coupled to an AC source.

Mehta teaches an apparatus for analyzing particles suspended in a fluid comprising electrodes (abstract) which can be used for electroporation (column 20, lines 30-66). Mehta discloses that "Precautions should be taken to avoid polarization of this small electrode. The effects of polarization can be reduced by using a high frequency AC voltage rather than DC

voltage, or by creating the constricted electrical path for a shorter duration" (column 7, lines 33-37).

At the time the invention was made, it would have been obvious to the person of ordinary skill in the art to have substituted DC voltage with AC voltage, thus resulting in an applied electric field wherein the polarity is periodically reversed and established from an AC source (such as a standard electrical wall outlet). One of ordinary skill in the art would have been motivated to do this in order to have avoided electrode polarization.

Additionally, Calvin differs from the claimed invention in that it does not expressly disclose the peak and average power consumptions, AC voltage, and current frequency. Nevertheless, the selection of specific suitable peak and average power consumptions, voltages, and current frequency, including those claimed, would have been an obvious matter of optimization on the part of the artisan of ordinary skill in the art, as the poration of cell membranes would have been affected by the applied electric field. Moreover, Calvin teaches that "the field strength at which maximum transformation occurs is determined by the cell type and the concentration at which the cells are suspended in the transformation buffer" (column 6, lines 61-64).

A holding of obviousness is clearly required.

Response to Arguments

Applicant's arguments filed April 18, 2008, have been fully considered but they are not persuasive. The applicant argues that the primary reference, Calvin, does not teach effecting electroporation while an electric field is substantially constant. In supporting this argument, the

applicant cites sections of column 8 of Calvin. However, it is respectfully noted that Calvin teaches that "...a potential of 600 volts DC **is maintained** by power source...on the electrodes within the chamber" (column 7, lines 58-62, emphasis added). Thus, the electric field is substantially constant in terms of magnitude, as required by claim 1. In terms of the cited sections of column 8, the electric field strength that falls off greatly is that "impressed upon the suspension" (column 8, lines 32-35). The recitation of the electric field magnitude in the instant claims is broad, and can be considered the electric field maintained on the electrodes. Specifically, the instant claims simply require that the electric field is substantially constant in terms of magnitude, not that the electric field impressed on the sample is constant in magnitude. Thus, Calvin does not teach away from the claimed invention.

While the teachings regarding polarization in Mehta are in reference to electrodes to distinguish a signal from noise, the teachings can be applied to all types of electrodes serving different purposes, including electroporation electrodes. Polarity reversal is indeed taught since AC voltages involve polarity reversal.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Claims 1, 3-8, and 12-16 are rejected. Claims 34 and 35 are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSAN E. FERNANDEZ whose telephone number is (571)272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford/
Primary Examiner, Art Unit 1651

Susan E. Fernandez
Examiner
Art Unit 1651

sef